```
Ala Cys Leu Leu Arg Leu Gly Thr Gln Gln Val Gly Pro Leu Gln Leu
                -5                   1                   5

His Thr Gly Ala Ser His Ala Ala Arg Asn His Tyr Glu Val Leu Val
        10                  15                  20

Leu Gly Gly Gly Ser Gly Gly Ile Thr Met Ala Ala Arg Met Lys Arg
    25                  30                  35

Lys Val Gly Ala Glu Asn Val Ala Ile Val Glu Pro Ser Glu Arg His
40                  45                  50                  55

Phe Tyr Gln Pro Ile Trp Thr Leu Val Gly Ala Gly Ala Lys Gln Leu
                60                  65                  70

Ser Ser Ser Gly Arg Pro Thr Ala Ser Val Ile Pro Ser Gly Val Glu
            75                  80                  85

Trp Ile Lys Ala Arg Val Thr Glu Leu Asn Gln Thr Arg Leu His His
        90                  95                  100

Thr Asp Asp Asp Gly
    105
```

(2) INFORMATION FOR SEQ ID NO: 315:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 101 amino acids
(B) TYPE: AMINO ACID
(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Umbilical cord

(ix) FEATURE:
(A) NAME/KEY: sig_peptide
(B) LOCATION: -86..-1
(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 5.5
seq ALLTGPTLGSSQA/RW

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 315:

```
Met Ser Glu Met Ala Glu Leu Ser Glu Leu Tyr Glu Glu Ser Ser Asp
    -85                 -80                 -75

Leu Gln Met Asp Val Met Pro Gly Glu Gly Asp Leu Pro Gln Met Glu
-70                  -65                 -60                 -55

Val Gly Ser Gly Ser Arg Glu Leu Ser Leu Arg Pro Ser Arg Ser Gly
                -50                 -45                 -40

Ala Gln Gln Leu Glu Glu Glu Gly Pro Met Glu Glu Glu Glu Ala Gln
            -35                 -30                 -25
```

```
Pro Met Ala Xaa Gln Arg Gly Asn Gly Ala Leu Leu Thr Gly Pro Thr
       -20                 -15                 -10

Leu Gly Ser Ser Gln Ala Arg Trp Arg Ala Xaa Thr Ser Arg Ala Arg
    -5                   1                   5                  10

Thr Arg Ala Pro Gly
                15
```

(2) INFORMATION FOR SEQ ID NO: 316:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 37 amino acids
(B) TYPE: AMINO ACID
(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Lymph ganglia

(ix) FEATURE:
(A) NAME/KEY: sig_peptide
(B) LOCATION: -15..-1
(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 5.3
seq IVSVLALIPXTTT/LT

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 316:

```
Met Leu Ile Val Ser Val Leu Ala Leu Ile Pro Xaa Thr Thr Thr Leu
-15                 -10                 -5                   1

Thr Val Gly Gly Gly Val Phe Ala Xaa Val Thr Ala Val Cys Cys Leu
              5                  10                  15

Ala Asp Gly Gly Gly
         20
```

(2) INFORMATION FOR SEQ ID NO: 317:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 50 amino acids
(B) TYPE: AMINO ACID
(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Lymph ganglia

(ix) FEATURE:
(A) NAME/KEY: sig_peptide

(B) LOCATION: -29..-1
(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 5
seq ELSLLPSSLWVLA/TS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 317:

```
Met Thr Cys Arg Gly Ser Cys Ser Tyr Ala Thr Arg Arg Ser Pro Ser
               -25                 -20                 -15

Glu Leu Ser Leu Leu Pro Ser Ser Leu Trp Val Leu Ala Thr Ser Ser
           -10                 -5                  1

Pro Thr Ile Thr Ile Ala Leu Ala Met Ala Ala Gly Asn Leu Cys Pro
     5                  10                  15

Leu Arg
 20
```

(2) INFORMATION FOR SEQ ID NO: 318:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 58 amino acids
(B) TYPE: AMINO ACID
(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Umbilical cord

(ix) FEATURE:
(A) NAME/KEY: sig_peptide
(B) LOCATION: -15..-1
(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 4.9
seq AVVFVFSLLDCCA/LI

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 318:

```
Met Glu Ala Val Val Phe Val Phe Ser Leu Leu Asp Cys Cys Ala Leu
-15                 -10                 -5                  1

Ile Phe Leu Ser Val Tyr Phe Ile Ile Thr Leu Ser Xaa Leu Glu Cys
               5                   10                  15

Asp Tyr Ile Asn Ala Arg Ser Cys Cys Ser Lys Leu Asn Lys Trp Val
          20                  25                  30

Ile Pro Glu Leu Ile Gly His Thr Ile Gly
     35                  40
```

(2) INFORMATION FOR SEQ ID NO: 319:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 57 amino acids
(B) TYPE: AMINO ACID
(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Lymph ganglia

(ix) FEATURE:
(A) NAME/KEY: sig_peptide
(B) LOCATION: -30..-1
(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 4.9
seq VAHALSLPAQSYG/ND

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 319:

```
Met Ala Ala Thr Ser Gly Thr Asp Glu Pro Val Ser Gly Glu Leu Val
-30                 -25                 -20                 -15

Ser Val Ala His Ala Leu Ser Leu Pro Ala Gln Ser Tyr Gly Asn Asp
               -10                 -5                  1

Pro Asp Ile Glu Met Ala Trp Ala Met Arg Ala Met Gln His Ala Glu
          5                  10                  15

Val Tyr Tyr Lys Leu Ile Ser Ser Val
     20                  25
```

(2) INFORMATION FOR SEQ ID NO: 320:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 44 amino acids
(B) TYPE: AMINO ACID
(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Lymph ganglia

(ix) FEATURE:
(A) NAME/KEY: sig_peptide
(B) LOCATION: -17..-1
(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 4.6
seq ALFLLLHNEMVSG/VY

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 320:

```
Met Ala Asp Glu Ala Leu Phe Leu Leu Leu His Asn Glu Met Val Ser
        -15                 -10                 -5
```

```
Gly Val Tyr Lys Ser Ala Xaa Xaa Gly Arg Trp Lys Thr Asp Asp Val
 1               5                  10                  15

Leu Leu Ser Trp Lys Thr Trp Gly Phe Glu Trp Asp
            20                  25
```

(2) INFORMATION FOR SEQ ID NO: 321:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 126 amino acids
(B) TYPE: AMINO ACID
(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Lymphocytes

(ix) FEATURE:
(A) NAME/KEY: sig_peptide
(B) LOCATION: -119..-1
(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 4.3
seq SVCLSIISMLSSC/KE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 321:

```
Met Ala Ser Met Gln Lys Arg Leu Gln Lys Glu Leu Leu Ala Leu Gln
               -115                 -110                 -105

Asn Asp Pro Pro Pro Gly Met Thr Leu Asn Glu Lys Ser Val Gln Asn
           -100                 -95                  -90

Ser Ile Thr Gln Trp Ile Val Asp Met Glu Gly Ala Pro Gly Thr Leu
       -85                  -80                  -75

Tyr Glu Gly Glu Lys Phe Gln Leu Leu Phe Lys Phe Ser Ser Arg Tyr
   -70                  -65                  -60

Pro Phe Asp Ser Pro Gln Val Met Phe Thr Gly Glu Asn Ile Pro Val
-55                  -50                  -45                  -40

His Pro His Val Tyr Ser Asn Gly His Ile Cys Leu Ser Ile Leu Thr
               -35                  -30                  -25

Glu Asp Trp Ser Pro Ala Leu Ser Val Gln Ser Val Cys Leu Ser Ile
           -20                  -15                  -10

Ile Ser Met Leu Ser Ser Cys Lys Glu Lys Arg Arg Pro Pro
       -5                   1                    5
```

(2) INFORMATION FOR SEQ ID NO: 322:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 59 amino acids

(B) TYPE: AMINO ACID
(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Lymph ganglia

(ix) FEATURE:
(A) NAME/KEY: sig_peptide
(B) LOCATION: -27..-1
(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 4.1
seq VLMFCVTPPELET/KX

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 322:

```
Met Lys Xaa Met Thr Gly Ser Glu Asn Trp Lys Thr Lys Lys Val Leu
      -25                 -20                 -15

Met Phe Cys Val Thr Pro Pro Glu Leu Glu Thr Lys Xaa Asn Ile Thr
  -10                 -5                   1                 5

Lys Gly Gly Leu Val Leu Phe Xaa Ala Asn Ser Asn Ser Ser Cys Met
               10                  15                  20

Glu Leu Ser Lys Lys Ile Ala Glu Arg Pro Ala
           25                  30
```

(2) INFORMATION FOR SEQ ID NO: 323:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 39 amino acids
(B) TYPE: AMINO ACID
(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Lymphocytes

(ix) FEATURE:
(A) NAME/KEY: sig_peptide
(B) LOCATION: -33..-1
(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 4.1
seq LFMTRTLCSPGPS/QP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 323:

```
Met Gln His Ile Val Gly Val Pro His Val Leu Val Arg Arg Gly Leu
          -30                 -25                 -20

Leu Gly Arg Asp Leu Phe Met Thr Arg Thr Leu Cys Ser Pro Gly Pro
      -15                 -10                  -5
```

Ser Gln Pro Arg Glu Ala Gly
1 5

(2) INFORMATION FOR SEQ ID NO: 324:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 68 amino acids
(B) TYPE: AMINO ACID
(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Lymph ganglia

(ix) FEATURE:
(A) NAME/KEY: sig_peptide
(B) LOCATION: -19..-1
(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 3.8
seq ALALASSQSHLLG/RD

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 324:

Met Tyr His Gln Ser Glu Ala Leu Ala Leu Ala Ser Ser Gln Ser His
-15 -10 -5

Leu Leu Gly Arg Asp Ser Pro Ser Ala Val Phe Glu Gln Asp Leu Glu
1 5 10

Asn Lys Glu Met Ser Lys Glu Trp Phe Leu Phe Asn Asp Ser Arg Val
15 20 25

Thr Phe Thr Ser Phe Gln Ser Val Gln Lys Ile Thr Ser Arg Phe Pro
30 35 40 45

Lys Asp Thr Trp

(2) INFORMATION FOR SEQ ID NO: 325:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 54 amino acids
(B) TYPE: AMINO ACID
(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Umbilical cord

(ix) FEATURE:
(A) NAME/KEY: sig_peptide
(B) LOCATION: -22..-1

(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 3.8
seq FASVAMICAIASG/SE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 325:

```
Met Ser Gly Gln Gly Leu Ala Gly Phe Phe Ala Ser Val Ala Met Ile
    -20                 -15                 -10

Cys Ala Ile Ala Ser Gly Ser Glu Leu Ser Glu Ser Ala Xaa Gly Tyr
 -5                  1                   5                  10

Phe Ile Thr Ala Cys Ala Val Ile Ile Leu Thr Ile Ile Cys Tyr Leu
                15                  20                  25

Gly Leu Pro Arg Gln Gly
            30
```

(2) INFORMATION FOR SEQ ID NO: 326:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 50 amino acids
(B) TYPE: AMINO ACID
(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Lymph ganglia

(ix) FEATURE:
(A) NAME/KEY: sig_peptide
(B) LOCATION: -30..-1
(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 3.7
seq SMMLLTVYGGYLC/SV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 326:

```
Met Pro Thr Gly Lys Gln Leu Ala Asp Ile Gly Tyr Lys Thr Phe Ser
-30                 -25                 -20                 -15

Thr Ser Met Met Leu Leu Thr Val Tyr Gly Gly Tyr Leu Cys Ser Val
                -10                 -5                  1

Arg Val Tyr His Tyr Phe Gln Trp Arg Arg Ala Gln Arg Xaa Ala Xaa
          5                  10                  15

Glu Gly
     20
```

(2) INFORMATION FOR SEQ ID NO: 327:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 18 amino acids
(B) TYPE: AMINO ACID
(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Lymph ganglia

(ix) FEATURE:
(A) NAME/KEY: sig_peptide
(B) LOCATION: -14..-1
(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 3.5
seq FPVCLTVTAAVCG/XX

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 327:

Met Phe Pro Val Cys Leu Thr Val Thr Ala Ala Val Cys Gly Xaa Xaa
-10 -5 1

Ala Gln

(2) INFORMATION FOR SEQ ID NO: 328:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 49 amino acids
(B) TYPE: AMINO ACID
(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Lymph ganglia

(ix) FEATURE:
(A) NAME/KEY: sig_peptide
(B) LOCATION: -15..-1
(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 3.5
seq VIFFACVVRVRDG/LP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 328:

Met Ser Val Ile Phe Phe Ala Cys Val Val Arg Val Arg Asp Gly Leu
-15 -10 -5 1

Pro Leu Ser Ala Ser Thr Asp Phe Tyr His Thr Gln Asp Phe Leu Glu
5 10 15

Trp Arg Arg Arg Leu Lys Ser Leu Ala Leu Arg Leu Ala Gln Tyr Pro
20 25 30

Gly

(2) INFORMATION FOR SEQ ID NO: 329:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 89 amino acids
(B) TYPE: AMINO ACID
(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Lymphocytes

(ix) FEATURE:
(A) NAME/KEY: sig_peptide
(B) LOCATION: -68..-1
(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 3.5
seq LVLDVVMLLLYLG/IE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 329:

```
Met Leu Xaa Gly Gly Leu Lys Met Ala Pro Arg Gly Lys Arg Leu Ser
            -65                 -60                 -55

Ser Thr Pro Leu Glu Ile Leu Phe Phe Leu Asn Gly Trp Tyr Asn Ala
        -50                 -45                 -40

Thr Tyr Phe Leu Leu Glu Leu Phe Ile Phe Leu Tyr Lys Gly Val Leu
    -35                 -30                 -25

Leu Pro Tyr Pro Thr Ala Asn Leu Val Leu Asp Val Val Met Leu Leu
-20                 -15                 -10                  -5

Leu Tyr Leu Gly Ile Glu Val Ile Arg Leu Phe Phe Gly Thr Lys Gly
                  1                   5                  10

Asn Leu Cys Gln Arg Lys Met Pro Arg
       15                  20
```

(2) INFORMATION FOR SEQ ID NO: 330:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 65 amino acids
(B) TYPE: AMINO ACID
(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Lymph ganglia

(ix) FEATURE:
(A) NAME/KEY: sig_peptide
(B) LOCATION: -36..-1

(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 3.5
seq PALTILHLPGTEG/VA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 330:

```
Met Ile Gly Gly Gly Arg Trp Asp Pro Pro Gly Ala Gln Ala Pro Ser
    -35                 -30                 -25

Ser Gln Ala Phe Pro Arg Arg Pro Ala Leu Thr Ile Leu His Leu Pro
-20                 -15                 -10                  -5

Gly Thr Glu Gly Val Ala Ser Gln Leu Thr Pro Ala Pro Lys Leu Ser
                  1               5                  10

Ser Ala Ala Gly Trp Leu Glu Val Pro Phe Asp Ala Ile Pro Ala Pro
         15                  20                  25

Gly
```

(2) INFORMATION FOR SEQ ID NO: 331:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 57 amino acids
(B) TYPE: AMINO ACID
(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Lymph ganglia

(ix) FEATURE:
(A) NAME/KEY: sig_peptide
(B) LOCATION: -28..-1
(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 8.4
seq LLRLLCLLPTGLP/VR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 331:

```
Met Val Arg Arg Val Gln Pro Asp Arg Lys Gln Leu Pro Leu Val Leu
            -25                 -20                 -15

Leu Arg Leu Leu Cys Leu Leu Pro Thr Gly Leu Pro Val Arg Ser Val
        -10                 -5                  1

Asp Phe Asn Arg Gly Thr Asp Asn Ile Thr Val Arg Gln Gly Asp Thr
  5                 10                  15                  20

Ala Ile Leu Arg Phe Leu Xaa Ser Gly
                  25
```

(2) INFORMATION FOR SEQ ID NO: 332:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 51 amino acids
(B) TYPE: AMINO ACID
(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Lymph ganglia

(ix) FEATURE:
(A) NAME/KEY: sig_peptide
(B) LOCATION: -19..-1
(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 7.4
seq LVFIIGLVGNLLA/LV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 332:

```
Met Pro Leu His Tyr Ser Leu Val Phe Ile Ile Gly Leu Val Gly Asn
               -15                 -10                  -5

Leu Leu Ala Leu Val Val Ile Val Gln Asn Arg Lys Lys Ile Asn Ser
            1               5                  10

Thr Thr Leu Tyr Ser Thr Asn Leu Val Ile Ser Asp Ile Leu Phe Xaa
     15                  20                  25

Thr Val Gly
 30
```

(2) INFORMATION FOR SEQ ID NO: 333:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 71 amino acids
(B) TYPE: AMINO ACID
(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Umbilical cord

(ix) FEATURE:
(A) NAME/KEY: sig_peptide
(B) LOCATION: -30..-1
(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 6.5
seq WATLGLLVAGLGG/HD

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 333:

```
Met Ala Arg Gly Leu Gly Ala Pro His Trp Val Ala Val Gly Leu Leu
-30                 -25                 -20                 -15
```

```
Thr Trp Ala Thr Leu Gly Leu Leu Val Ala Gly Leu Gly Gly His Asp
                -10                 -5                   1

Asp Leu His Asp Asp Leu Gln Glu Asp Phe His Gly His Ser His Arg
          5                  10                  15

His Ser His Glu Asp Phe His His Gly Xaa Ser His Ala His Gly His
     20                  25                  30

Gly His Xaa His Glu Ser Met
 35                  40
```

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(57) Abstract

The sequences of 5' ESTs derived from mRNAs encoding secreted proteins are disclosed. The 5' ESTs may be to obtain cDNAs and genomic DNAs corresponding to the 5' ESTs. The 5' ESTs may also be used in diagnostic, forensic, gene therapy, and chromosome mapping procedures. Upstream regulatory sequences may also be obtained using the 5' ESTs. The 5' ESTs may also be used to design expression vectors and secretion vectors.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 98/01237

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/12 C07K14/47 C12N15/10 C12N15/11

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ADAMS M D ET AL: "INITIAL ASSESSMENT OF HUMAN GENE DIVERSITY AND EXPRESSION PATTERNS BASED UPON 83 MILLION NUCLEOTIDES OF CDNA SEQUENCE" NATURE, vol. 377, no. SUPPL, 28 September 1995, pages 3-17, XP002069461	3-8, 15-19, 21,24,27
Y	see the whole document	12-14, 29-32, 35-37
	-& DATABASE EMBL - EMEST14 Entry HSZZ87788, Acc.No. AA382642, 18 April 1997 ADAMS, M.D. ET AL.: "EST95896 Testis I Homo spaiens cDNA 5' end." XP002083842 see the whole document -& DATABASE EMBL - EMEST14 Entry HSZZ86710, Acc.No. AA381563, -/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

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Date of the actual completion of the international search	Date of mailing of the international search report
10 November 1998	08.02.99
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Smalt, R

1

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	18 April 1997 ADAMS, M.D. ET AL.: "EST94680 ACtivated T-cell I Homo sapiens CDNA 5' end." XP002083843 see the whole document	
Y	EP 0 279 582 A (BAYLOR COLLEGE MEDICINE) 24 August 1988 see the whole document	12,13
Y	LIN Y ET AL: "INHIBITION OF NUCLEAR TRANSLOCATION OF TRANSCRIPTION FACTOR NF-KB BY A SYNTHETIC PEPTIDE CONTAINING A CELL MEMBRANE-PERMEABLE MOTIF AND NUCLEAR LOCALIZATION SEQUENCE" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 270, no. 24, 16 June 1995, pages 14255-14258, XP002050723 see the whole document	14
Y	GREENWOOD M T ET AL: "Cloning of the gene encoding human somatostatin receptor 2: sequence analysis of the 5'-flanking promoter region" GENE, vol. 159, no. 2, 4 July 1995, page 291-292 XP004042228	29-32
A	see the whole document	33
Y	LOCKHART D J ET AL: "EXPRESSION MONITORING BY HYBRIDIZATION TO HIGH-DENSITY OLIGONUCLEOTIDE ARRAYS" BIO/TECHNOLOGY, vol. 14, no. 13, December 1996, pages 1675-1680, XP002022521 see the whole document	35-37
A	HEIJNE VON G.: "A new method for predicting signal sequence cleavage sites" NUCLEIC ACIDS RESEARCH, vol. 14, no. 11, 1986, pages 4683-4690, XP002053954 cited in the application	12
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1

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 98/01237

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 625 572 A (KANAGAWA ACAD OF SCIENCE AND TECHNOL FOUNDATION (JP); KATO S; SEKINE S) 23 November 1994 cited in the application	
A	CARNINCI P. ET AL.: "High-efficiency full-length cDNA cloning by biotinylated CAP trapper" GENOMICS, vol. 37, no. 3, 1 November 1996, pages 327-336, XP002081729 cited in the application	
A	WO 97 07198 A (GENETICS INSTITUTE INC (US); JACOBS K; MCCOY JM; KELLEHER K; CARLIN M) 27 February 1997	
A	TASHIRO K. ET AL.: "Signal sequence trap: a cloning strategy for secreted proteins and type I membrane proteins" SCIENCE, vol. 261, 30 July 1993, pages 600-603, XP000673204	
A	YOKOYAMA-KOBAYASHI M. ET AL.: "A signal sequence detection system using secreted protease activity as an indicator" GENE, vol. 163, 1995, pages 193-196, XP002053953	
P,X	DATABASE EMBL - EMEST3 Entry/Acc.No. AA805310., 16 February 1998 STRAUSBERG, R.: "oc15a05.s1 NCI_CGAP_GCB1 Homo spaiens cDNA clone IMAGE:1340912." XP002083844 see the whole document	3-8

1

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Inte. .tional application No.
PCT/IB 98/01237

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-37 partially (Invention 1. on continuation-sheet)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: Invention 1: claims 1-37 all partially

Nucleic acid comprising the sequence as in Seq.ID:38, complementary sequence, fragments, hybridizing sequences. Polypeptide comprising a signal peptide encoded by said nucleotide sequence. Vector encoding a fusion protein comprising said signal peptide. A method of directing the extracellular secretion of a polypeptide by means of said vector. Method of importing a polypeptide into a cell by means of said signal peptide. A method for making a cDNA encoding a secretory protein, partially encoded by said nucleotide sequence, corresponding cDNA. Polypeptide encoded by said nucleotide sequence, comprising a sequence as in Seq.ID:186, method of making said polypeptide. Method of obtaining a promoter located upstream of said nucleotide sequence, promoter thereof.

2. Claims: Inventions 2-147: claims 1-37 all partially

Inventions 2-147: Idem as subject 1 but limited to each of the DNA sequences as in Seq.ID:39-185, and corresponding polypeptides, where invention 2 is limited to Seq.ID:39 and 187, invention 3 is limited to Seq.ID:40 and 188,....., invention 147 is limited to Seq.ID:185 and 333).

For the sake of conciseness, the first subject matter is explicitly defined, the other subject matters are defined by analogy thereto.

INTERNATIONAL SEARCH REPORT

ormation on patent family members

Inter ɔnal Application No
PCT/IB 98/01237

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		WO 9704097 A	06-02-1997

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A3

(11) International Publication Number: **WO 99/06553**

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08/905,051 1 August 1997 (01.08.97) US

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(74) Agents: MARTIN, Jean–Jacques et al.; Cabinet Regimbeau, 26, avenue Kléber, F–75116 Paris (FR).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.
With amended claims.

(88) Date of publication of the international search report:
8 April 1999 (08.04.99)

Date of publication of the amended claims:
27 May 1999 (27.05.99)

(54) Title: 5' ESTs FOR SECRETED PROTEINS EXPRESSED IN VARIOUS TISSUES

(57) Abstract

The sequences of 5' ESTs derived from mRNAs encoding secreted proteins are disclosed. The 5' ESTs may be to obtain cDNAs and genomic DNAs corresponding to the 5' ESTs. The 5' ESTs may also be used in diagnostic, forensic, gene therapy, and chromosome mapping procedures. Upstream regulatory sequences may also be obtained using the 5' ESTs. The 5' ESTs may also be used to design expression vectors and secretion vectors.

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AMENDED CLAIMS
[received by the International Bureau on 8 April 1999 (08.04.99);
original claims 1-37 amended (5 pages)]

1. A purified or isolated nucleic acid comprising the sequence of one of SEQ ID NOs: 38-185 or comprising a sequence complementary thereto.

2. The nucleic acid of Claim 1, wherein said nucleic acid is recombinant.

3. A purified or isolated nucleic acid comprising at least 10 consecutive bases of the sequence of one of SEQ ID NOs: 38-185 or one of the sequences complementary thereto, with the exception of a purified or isolated nucleic acid consisting of consecutive bases which are situated entirely in the sequences identified as Feature in the corresponding SEQ ID under key:other.

4. A purified or isolated nucleic acid comprising at least 15 consecutive bases of one of the sequences of SEQ ID NOs: 38-185 or one of the sequences complementary thereto, with the exception of a purified or isolated nucleic acid consisting of consecutive bases which are situated entirely in the sequences identified as Feature in the corresponding SEQ ID under key:other.

5. The nucleic acid of Claim 4, wherein said nucleic acid is recombinant.

6. A purified or isolated nucleic acid of at least 15 bases capable of hybridizing under stringent conditions to the sequence of one of SEQ ID NOs: 38-185 or one of the sequences complementary to the sequences of SEQ ID NOs: 38-185, with the exception of a purified or isolated nucleic acid consisting of consecutive bases which are situated entirely in the sequences identified as Feature in the corresponding SEQ ID under key:other.

7. The nucleic acid of Claim 6, wherein said nucleic acid is recombinant.

8. A purified or isolated nucleic acid encoding a human gene product, said human gene product having a sequence partially encoded by one of the sequences of SEQ ID NO: 38-185, with the exception of a purified or isolated nucleic acid consisting of consecutive bases which are situated entirely in the sequences identified as Feature in the corresponding SEQ ID under key:other.

9. A purified or isolated nucleic acid having the sequence of one of SEQ ID NOs: 38-185 or having a sequence complementary thereto.

10. A purified or isolated nucleic acid comprising the nucleotides of one of SEQ ID NOs: 38-185 which encode a signal peptide.

11. A purified or isolated polypeptides comprising a signal peptide encoded by one of the sequences of SEQ ID NOs: 38-185.

12. A vector encoding a fusion protein comprising a polypeptide and a signal peptide, said vector comprising a first nucleic acid encoding a signal peptide encoded by one of the sequences of SEQ ID NOs: 38-185 operably linked to a second nucleic acid encoding a polypeptide.

13. A method of directing the extracellular secretion of a polypeptide or the insertion of a polypetide into the membrane comprising the steps of:

obtaining a vector according to Claim 12; and

introducing said vector into a host cell such that said fusion protein is secreted into the extracellular environment of said host cell or inserted into the membrane of said host cell.

14. A method of importing a polypeptide into a cell comprising contacting said cell with a fusion protein comprising a signal peptide encoded by one of the sequences of SEQ ID NOs: 38-185 operably linked to said polypeptide.

15. A method of making a cDNA encoding a human secretory protein that is partially encoded by one of SEQ ID NOs 38-185, comprising the steps of:

obtaining a cDNA comprising one of the sequences of SEQ ID NOs: 38-185;

contacting said cDNA with a detectable probe comprising at least 15 consecutive nucleotides of said sequence of SEQ ID NO: 38-185 or a sequence complementary thereto under conditions which permit said probe to hybridize to said cDNA;

identifying a cDNA which hybridizes to said detectable probe; and

isolating said cDNA which hybridizes to said probe.

16. An isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein encoded by one of SEQ ID NOs 38-185 or a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method of Claim 15.

17. The cDNA of Claim 16 wherein said cDNA comprises the full protein coding sequence partially included in one of the sequences of SEQ ID NOs: 38-185.

18. A method of making a cDNA comprising one of the sequences of SEQ ID NOs: 38-185, comprising the steps of:

contacting a collection of mRNA molecules from human cells with a first primer capable of hybridizing to the polyA tail of said mRNA;

hybridizing said first primer to said polyA tail;

reverse transcribing said mRNA to make a first cDNA strand;

making a second cDNA strand complementary to said first cDNA strand using at least one primer comprising at least 15 nucleotides of one of the sequences of SEQ ID NOs 38-185; and

isolating the resulting cDNA comprising said first cDNA strand and said second cDNA strand.

19. An isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein encoded by one of SEQ ID NOs 38-185 or a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method of Claim 18.

20. The cDNA of Claim 19 wherein said cDNA comprises the full protein coding sequence partially included in one of the sequences of SEQ ID NOs: 38-185.

21. The method of Claim 18, wherein the second cDNA strand is made by:

contacting said first cDNA strand with a first pair of primers, said first pair of primers comprising a second primer comprising at least 15 consecutive nucleotides of one of the sequences of SEQ ID NOs 38-185 and a third primer having a sequence therein which is included within the sequence of said first primer;

performing a first polymerase chain reaction with said first pair of nested primers to generate a first PCR product;

contacting said first PCR product with a second pair of primers, said second pair of primers comprising a fourth primer, said fourth primer comprising at least 15 consecutive nucleotides of said sequence of one of SEQ ID NO:s 38-185 , and a fifth primer, said fourth and fifth primers being capable of hybridizing to sequences within said first PCR product; and

performing a second polymerase chain reaction, thereby generating a second PCR product.

22. An isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein encoded by one of SEQ ID NOs 38-185, or a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method of Claim 21.

23. The cDNA of Claim 22 wherein said cDNA comprises the full protein coding sequence partially included in one of the sequences of SEQ ID NOs: 38-185.

24. The method of Claim 18 wherein the second cDNA strand is made by:

contacting said first cDNA strand with a second primer comprising at least 15 consecutive nucleotides of the sequences of SEQ ID NOs: 38-185;

hybridizing said second primer to said first strand cDNA; and

extending said hybridized second primer to generate said second cDNA strand.

25. An isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein partially encoded by one of SEQ ID NOs 38-185 or comprising a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method of Claim 24.

26. The cDNA of Claim 25, wherein said cDNA comprises the full protein coding sequence partially included in of one of the sequences of SEQ ID NOs: 38-185.

27. A method of making a protein comprising one of the sequences of SEQ ID NO: 186-333, comprising the steps of:

obtaining a cDNA encoding the full protein sequence partially included in one of the sequences of sequence of SEQ ID NO: 38-185;

inserting said cDNA in an expression vector such that said cDNA is operably linked to a promoter;

introducing said expression vector into a host cell whereby said host cell produces the protein encoded by said cDNA; and

isolating said protein.

28. An isolated protein obtainable by the method of Claim 27.

29. A method of obtaining a promoter DNA comprising the steps of:

obtaining DNAs located upstream of the nucleic acids of SEQ ID NO: 38-185 or the sequences complementary thereto;

screening said upstream DNAs to identify a promoter capable of directing transcription initiation; and

isolating said DNA comprising said identified promoter.

30. The method of Claim 29, wherein said obtaining step comprises chromosome walking from said nucleic acids of SEQ ID NO: 38-185 or sequences complementary thereto.

31. The method of Claim 30, wherein said screening step comprises inserting said upstream sequences into a promoter reporter vector.

32. The method of Claim 30, wherein said screening step comprises identifying motifs in said upstream DNAs which are transcription factor binding sites or transcription start sites.

33. An isolated promoter obtainable by the method of Claim 32.

34. An isolated or purified protein comprising one of the sequences of SEQ ID NO: 186-333.

35. In an array of discrete ESTs or fragments thereof of at least 15 nucleotides in length, the improvement comprising inclusion in said array of at least one of the sequences of SEQ ID NOs: 38-185, or one of the sequences complementary to the sequences of SEQ ID NOs: 38-185, or a fragment thereof of at least 15 consecutive nucleotides.

36. The array of Claim 35 including therein at least two of the sequences of SEQ ID NOs: 38-185, the sequences complementary to the sequences of SEQ ID NOs: 38-185, or fragments thereof of at least 15 consecutive nucleotides.

37. The array of Claim 35 including therein at least five of the sequences of SEQ ID NOs: 38-185, the sequences complementary to the sequences of SEQ ID NOs: 38-185, or fragments thereof of at least 15 consecutive nucleotides.